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| APPLICATION NO.                                                      | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.  | CONFIRMATION NO. |
|----------------------------------------------------------------------|-------------|----------------------|----------------------|------------------|
| 09/913,325                                                           | 08/10/2001  | Martin Gleave        | UBC.P-020            | 8469             |
| 57381                                                                | 7590        | 11/14/2006           | EXAMINER             |                  |
| Marina Larson & Associates, LLC<br>P.O. BOX 4928<br>DILLON, CO 80435 |             |                      | VIVLEMORE, TRACY ANN |                  |
|                                                                      |             |                      | ART UNIT             | PAPER NUMBER     |
|                                                                      |             |                      | 1635                 |                  |

DATE MAILED: 11/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                                      |                                      |  |
|------------------------------|--------------------------------------|--------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>09/913,325 | <b>Applicant(s)</b><br>GLEAVE ET AL. |  |
|                              | <b>Examiner</b><br>Tracy Vivlemore   | <b>Art Unit</b><br>1635              |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 30 August 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 6,8-17 and 29-34 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 6,8,10,12-17,31 and 32 is/are rejected.
- 7) ☒ Claim(s) 9,11,29,30,33 and 34 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |                                                                                                            |                                                                                         |
|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                           | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>declaration of 8/30/06</u>             |

### **DETAILED ACTION**

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Response to argument: Claim Rejections - 35 USC § 103***

Claims 6, 8, 10, 12-17, 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bruchovsky et al. in view of Sensibar et al., Kyprianou et al. and Raghavan et al. This rejection is maintained for the reasons set forth in the office action mailed March 30, 2006.

Applicants traverse the 103 rejection by arguing that a rejection under obviousness requires more than just locating the pieces in the art. Applicants further asserts that the statement in Bruchovsky relied upon by the examiner is not a basis for finding a reasonable expectation of success. While applicant is correct that an obviousness rejection requires more than locating pieces in the prior art, it is noted that the reasonable expectation of success is not based solely on Bruchovsky, but also on Sensibar. A 103 rejection does not require absolute predictability, only a reasonable expectation of success. In the instant case the person of ordinary skill in the art would have a reasonable expectation of success in combining androgen withdrawal and antisense oligonucleotide gene therapy because of the teaching of Bruchovsky et al. that androgen withdrawal is a routine treatment for prostate cancer and the suggestion to combine this with TRPM-2 gene therapy, a therapy known in the art as evidenced by the teachings of Sensibar et al.

Applicants submit a declaration by inventor Gleave. In this declaration, Dr. Gleave argues in paragraph 3 that the statement relied upon by the examiner as

providing a motivation to combine the cited references indicated a direction that research would take, not a statement that anti-TRPM-2 would necessarily provide a therapeutic benefit. Dr. Gleave states that at the time it was not known whether a decrease in TRPM-2 levels would cause or prevent apoptosis. The examiner acknowledges that the effect of a decrease in TRPM-2 on apoptosis might not have been known, but this is not required by the claims, which recite that the TRPM-2 antisense inhibits expression of TRPM-2. Dr. Gleave further argues that the suggestion in the Bruchovsky paper does not provide an expectation of any particular result. This appears to be an argument that there is no reasonable expectation of success in the combination of the references. As discussed above, a reasonable expectation of success for a 103 rejection does not require absolute predictability.

Dr. Gleave further states that, as taught in the specification, the role of TRPM-2 was ambiguous and no clearly defined role for this protein was known, citing teachings from Sensibar reference to provide evidence that the role of TRPM-2 was unknown and noting that Sensibar specifically teaches the role of TPRM-2 in cell death was unknown. This is acknowledged, however, Sensibar is not relied upon for teaching the role of TRPM-2, but for a teaching that anti-TRPM-2 gene therapy, suggested as a possible treatment in Bruchovsky, was known to the person of ordinary skill in the art at the time of invention. While the precise role of TRPM-2 might have been unknown, the teachings of Bruchovsky show that tumor progression appears linked in part to inappropriate activation of the TRPM-2 gene.

Dr. Gleave further states his belief in paragraph 6 that the outcome of the proposed experiment combining antisense therapy and cyclic androgen withdrawal

could not have reasonably been predicted. This opinion is acknowledged but contradicts the suggestion presented in the Bruchovsky reference that this was a viable future direction for research. It is noted that the Bruchovsky appeared in a peer-reviewed journal and its content was subjected to review by other experts in the field who apparently concurred with applicant's suggestion that combination therapy would be a viable research path.

Dr. Gleave further states that nothing in the art would have predicted the synergistic effect of combinations of antisense to TRPM-2 and chemotherapy agents and provides data showing that while antisense alone does not appear to have any effect on tumor volume, a combination therapy is quite effective at reducing tumor volume. This data, while interesting because it provides evidence that antisense therapy alone is not an effective treatment for prostate cancer, is not probative evidence of non-obviousness of the instant claims because it is not commensurate with the claims. The claims require initiation of androgen withdrawal prior to antisense treatment while the data presented describes experiments using a combination of antisense and chemotherapeutic agent without mentioning androgen withdrawal.

Applicants further traverse the rejection with regard to the application of the Raghavan reference, asserting that because the reference teaches the combination of paclitaxel with other spindle inhibitors it offers no teaching or suggestion with respect to combination therapies generally. While Raghavan does specifically teach paclitaxel in combination with spindle inhibitors, this is not the only reference that teaches combination therapies. As described in the rejection, Bruchovsky et al. also teach that combination therapies using cytotoxic agents was known in the art at the time of

invention and suggest their use in treatment of prostate cancer. Based on the combined teachings of the art, one of ordinary skill would be motivated to use combination therapies and would have a reasonable expectation of success that they would be effective.

***Allowable Subject Matter***

Claims 9, 11, 29, 30, 33 and 34 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The central FAX Number is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore  
Examiner  
Art Unit 1635

TV  
November 1, 2006

  
JAMES SCHULTZ, PH.D.  
PRIMARY EXAMINER